2024 Horizon Scanning Forum

Medicines of Tomorrow

Medicines Australia

Acknowledgement of country

We acknowledge the traditional custodians of the lands on which we research and work, and we pay our respects to the Elders past, present and future.

We recognise and respect their cultural heritage, beliefs and continuous relationship with the land.

Acknowledgements

This report would not have been possible without the contribution of all our speakers, session chairs, and delegates.

We also thank Penny Shakespeare, Deputy Secretary of the Department of Health and Aged Care for undertaking the co-emcee role with Liz de Somer, CEO of Medicines Australia.

We extend our appreciation to the Horizon Scanning Forum Action Group and the Medicines Australia team who delivered this year's event.

L-R: Penny Shakespeare, Dr Anna Lavelle AM, the Hon Ged Kearney MP, Liz de Somer

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Foreword

Horizon scanning plays a vital role in helping to prepare Australia's regulatory and reimbursement systems for advances in therapies and medical breakthroughs so that patients have fast access to the best medicines available.

Medicines Australia's second Horizon Scanning Forum highlighted the urgent need for Health Technology Assessment (HTA) reform to accommodate new therapies that are not years away but entering the market now.

Lack of adequate horizon scanning over the last decade has contributed to the situation Australia is in today, where science and innovation has significantly outpaced our health system, to the detriment of patients. It is unacceptable that it currently takes 466 days on average from the time a new medicine is registered by the TGA to when it is made available to Australians on the Pharmaceutical Benefits Scheme (PBS).[1] This delay is the result of a system that was not designed to accommodate the medicines of today, or tomorrow, and needs urgent reform.

We are now in an era of unprecedented and accelerating innovations within the pharmaceutical and biotechnology sectors. It is imperative our regulatory, reimbursement and health systems are readied, and remain agile and flexible to accommodate future advances we cannot yet predict but will inevitably emerge.

This was demonstrated in the presentations by leading researchers and industry, which offered valuable insights for the leaders of our regulatory and reimbursement systems, and delegates from across our state and territory health departments, hospitals, research facilities, clinician and patient advocacy groups.

I extend my sincere thanks to the Hon. Ged Kearney MP, Assistant Minister for Health and Aged Care, for her thought-provoking opening address at the Forum, and to Penny Shakespeare, Deputy Sectretary, Department of Health and Aged Care, who co-chaired the event. The positive engagement from Government and the Department of Health and Aged Care (DoHAC) is welcomed by industry and we will continue to work collaboratively to develop a modern horizon scanning process to improve outcomes for patients.

Medicines Australia thanks our members and stakeholders, whose invaluable contribution helped to shape this year's forum from planning sessions to delivering presentations, sharing personal experience and actively participating in the event.

We thank the patient advocates who participated in the Forum and acknowledge their tireless work in advocating for faster access to medicines and a better healthcare system.

Liz de Somer

Chief Executive Officer

Executive summary

The Commonwealth and Medicines Australia have a shared ambition to promote greater understanding and insight into the new and emerging medicines, vaccines and biopharmaceuticals coming through development pipelines to ultimately facilitate faster access to new medicines for Australians.

Under Medicines Australia's Strategic Agreement with the Commonwealth, we convene an annual Horizon Scanning forum to identify major therapeutic advances which may represent a significant disruption in the treatment paradigm and/or require innovation in health care system planning; and to highlight potential implications for the Commonwealth from the introduction of these advances in terms of resources, systems and processes.

The 2024 Horizon Scanning Forum was curated in the context of Australia's first Health Technology Assessment Policy and Methods review (HTA Review) in more than 30 years nearing completion. The first round of consultations had concluded and in January 2024 an Options Paper was released to inform the second and final round of consultations. The need for a more rigorous Horizon Scanning system was identified in the Options Paper.

Continuing with the theme of our first Horizon Scanning Forum held in 2022 Medicines Australia identified four therapeutic areas where innovative new classes of medicines and treatments stand to disrupt treatment paradigms in Australia and require innovation in system planning. These were: cell and gene therapies, vaccine technology for infectious diseases, novel antimicrobials, and digital health.

The Forum comprised presentations and panel discussions on each of these therapeutic areas involving innovative pharmaceutical companies, research experts, patients and patient advocacy groups, to illustrate the experiences of different stakeholders within the system.

Consistent themes emerged across each session, underscoring the need for innovation in the regulation, reimbursement, and delivery of medicines, vaccines, and biopharmaceuticals. This report highlights the emerging technologies presented at the Horizon Scanning Forum, explores their implications for the health system, and summarises them into the following key takeaway messages:

Theme 1: Disruptive therapeutic advances present amazing opportunities for patients – but we must prepare the system now.

The presentations and discussions across each of the four therapeutic areas made evident that the health system, regulatory and reimbursement policies and processes must be reformed now, to enable timely access to these new technologies. Many of the therapies discussed are being introduced overseas and Australian patients will miss out on accessing timely treatment because our regulatory and reimbursement system is lagging.

Theme 2: A co-designed horizon scanning process, with input from all stakeholders, will help to identify unmet needs and enable system readiness to support timely access to new therapies.

Robust horizon scanning is critically important to enable effective planning for regulatory processes, HTA and health systems, so that patients can access new therapies as they become available. There are many stakeholders with a strong interest in horizon scanning as evidenced by the delegates who attended the Horizon Scanning Forum, including Commonwealth and State Government representatives, public and private hospital leaders, clinicians, researchers, patient groups and industry. For Australia to reap the benefits of truly effective horizon scanning, input from all stakeholders through a co-design process will be important.

In addition, Government commitment to reform, additional resourcing and measures to enhance workforce capability will be required.

Theme 3: The recently completed HTA Review has provided some good options to take horizon scanning forward in partnership.

Discussion across each of the four therapeutic areas highlighted the need and potential benefit of a nationally coordinated horizon scanning system and process, and the urgent need for broader HTA reforms, so that Australia can capitalise on the full potential of accelerating innovations in medicines, vaccines and biopharmaceuticals.

Medicines Australia supports the coordinated implementation of all three horizon scanning priorities proposed in the HTA Review Options Paper. These are:

- For advanced therapies and other potentially disruptive technologies.
- To meet priority areas (including addressing equity and high unmet clinical need).
- To help operational and capacity planning for HTA and health systems.[2]

Strong interest in horizon scanning across health

The Forum attracted more than 230 delegates in-person and online, a significant increase on attendee numbers in 2022 and clear evidence of strong interest in Horizon Scanning across the healthcare industry.

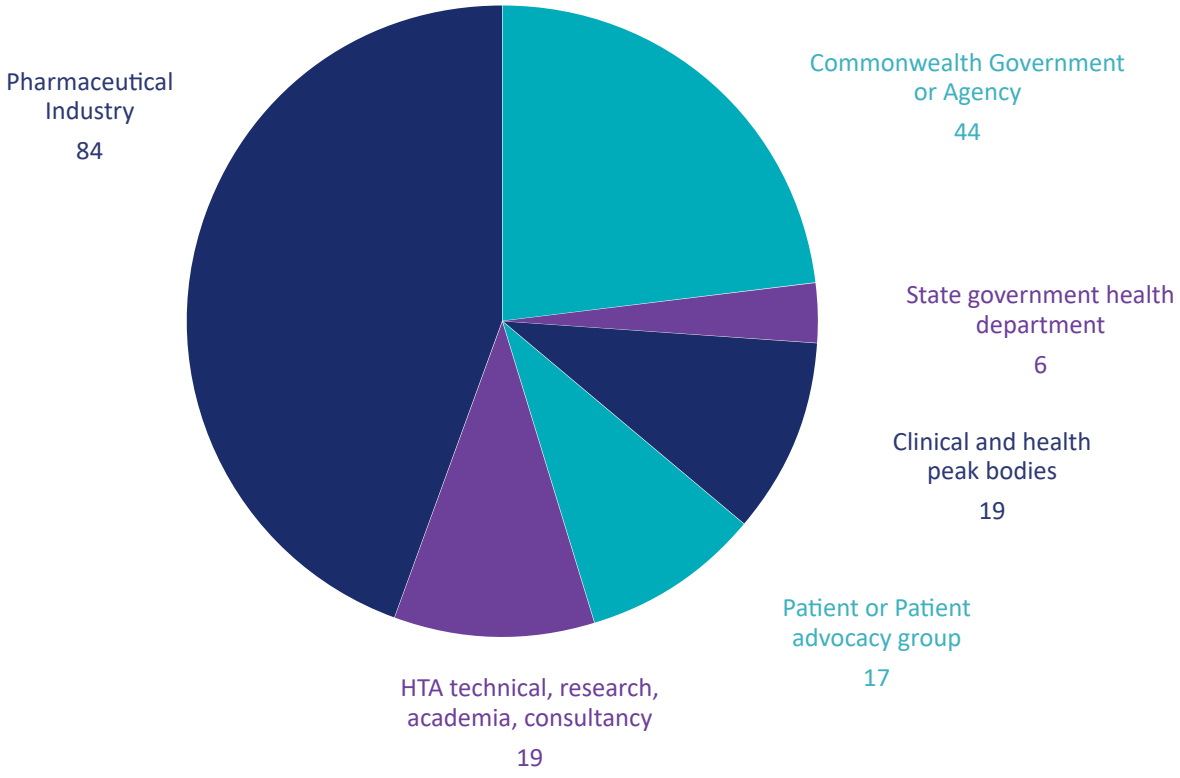
Senior executive representation from government agencies included:

- The Australian Government Chief Medical Officer.
- Deputy Secretary of the Health Resourcing Division of the DoHAC.
- Deputy Secretary of the Therapeutic Goods Administration (TGA).
- Chair of the Pharmaceutical Benefits Advisory Committee (PBAC).
- Chief Scientist of Australia.
- Chief Scientist of Western Australia (WA).
- Deputy Lead of the Minimising Antimicrobial Resistance (AMR) Mission of CSIRO.

Other delegates included:

- CEOs and representatives from 15 patient groups.
- Senior representatives from health and industry government departments in NSW, QLD, VIC, ACT and WA, including the Acting Chief Medical Officer and Acting Chief Pharmacist of the ACT.
- Representatives from the Royal Adelaide Hospital, Royal Perth Hospital, Mater Services Brisbane, Westmead Hospital, Peter MacCallum Cancer Centre, and Epworth Healthcare.
- Managing directors and representatives from pharmaceutical industry and life sciences stakeholders such as MTP Connect.

Figure 1: Number of in-person attendees by organisation type (N=189)



Medicines Australia will continue to work in partnership with the Commonwealth Government to progress horizon scanning, and keep stakeholders informed of major therapeutic advances as we move through this remarkable new era of medical research and therapy development.

Introduction

Welcome & opening remarks
Ms Liz de Somer, Chief Executive Officer, Medicines Australia

Address from Assistant Minister for Health
The Hon Ged Kearney MP

The Horizon Scanning scene
Ms Penny Shakespeare, Deputy Secretary, Department of Health and Aged Care

The patient voice
Ms Ann Single, The Patient Voice Initiative

Horizon scanning internationally and in Australia

Emerging in Europe in the 1980s, horizon scanning was initially the first step in HTA. Today, horizon scanning is defined by the HTA community as "the systematic identification of health technologies that are new, emerging, or becoming obsolete and that have the potential to affect health, health services, and/or society."[4]

Globally, several HTA agencies perform horizon scanning for medicines, vaccines, and biotechnology for a range of purposes, including:

- Identify interventions for unmet needs.
- Pinpoint innovations that could significantly impact clinical care, healthcare systems, patient outcomes, and costs.
- Ensure timely access to affordable, high-quality medicines.
- Improve patient access to innovative therapies and supporting sustainable national health systems.

While national-level horizon scanning for emerging technologies is undertaken in other nations, Australia currently does not have a robust and coordinated system in place. National horizon scanning activities in Australia peaked between 2003 to 2017 when the New Zealand Horizon Scanning Network (ANZHSN) functioned as the primary national horizon scanning body in Australia.[5]

Under Medicines Australia's Strategic Agreement with the Commonwealth 2022-2027, Medicines Australia hosts an annual Horizon Scanning Forum to promote greater understanding and insight into new and emerging medicines, vaccines and biopharmaceuticals coming through development pipelines and set to enter the Australian regulatory and / or reimbursement system in the next two to three years.

The inaugural December 2022 forum highlighted emerging therapeutics for mental health, Duchenne muscular dystrophy, Alzheimer's disease, and cancer. Discussions included the merits of nationally coordinated horizon scanning, co-designing a fit-for-purpose process, and acting on horizon scanning findings.

Therapy areas presented at the 2024 Horizon Scanning Forum

The 2024 Horizon Scanning Forum was curated in the context of Australia's first Health Technology Assessment (HTA) Policy and Methods Review (HTA Review) in more than 30 years nearing completion. The topics selected for presentation offered a macro view of emerging therapies that are already challenging the existing HTA system.

Specifically, the 2024 Forum focused on four broad therapeutic and technology areas: cell and gene therapy, novel vaccines for infectious diseases, novel antimicrobials, and digital health.

Medicines Australia member companies were invited, through an expressions of interest process, to showcase their emerging technologies related to one of the four therapy areas. Relevant experts, government representatives and patient advocates also presented and participated in panel discussions at each of the four therapy area sessions.

The therapeutic areas were identified by Medicines Australia through desktop literature search, and consultation with member companies and experts in the field. They represented areas of high unmet need and/or are emerging therapies that have the potential to disrupt health systems, regulatory and/ or reimbursement policies and processes.

Novel technology to prevent infectious diseases was identified as a key topic for the Forum, reflecting a new era of infectious disease, characterised by outbreaks of emerging, re-emerging and endemic pathogens.

Antimicrobial resistance (AMR) is one of the top global public health and development threats facing human health. This session looked at the challenges of AMR, potential regulatory and reimbursement reforms, and new antimicrobial therapies in development.

Cell and gene therapies (CGTs) are revolutionising medicine and have significant potential to transform patient outcomes. This session demonstrated that healthcare systems and processes must adapt, to ensure Australians will benefit from these new technologies in efficient, patient centric healthcare delivery models.

Digital health is revolutionising the global pharmaceutical industry and healthcare more generally, using artificial intelligence (AI), big data analytics and machine learning in the development of biotherapeutic products, pharmaceuticals and vaccines. Discussions explored the regulation, funding, and delivery of these technologies to patients.

Consistent themes emerged across each session, underscoring the need for innovation in the regulation, reimbursement, and delivery of medicines, vaccines, and biopharmaceuticals. This report highlights the emerging therapies presented at the Horizon Scanning Forum, explores their implications for the health system, and summarises them into the following themes:

Theme 1: Disruptive therapeutic advances present amazing opportunities for patients – but we must prepare the system now.

Theme 2: A co-designed horizon scanning process would better identify unmet needs and enable system readiness to support timely access to new therapies.

Theme 3: The HTA Review has provided some good options to take horizon scanning forward in partnership.

Theme 1. Disruptive therapeutic advances present amazing opportunities for patients – but we must prepare the system now

Medicines are crucial to healthcare, helping Australians live longer, healthier lives. There is growing evidence that investment in healthcare is an investment in valuable social and economic outcomes. Increased investment in health over the last two decades has positively impacted health outcomes, particularly life expectancy, as well as social and economic outcomes.[6]

With the unprecedented and accelerating innovations in pharmaceutical and biotechnology therapies, proactive decision making on where and how we invest in the health of Australians should be made now in readiness for the therapies of the future. This includes preparation and investment in our regulatory, reimbursement and health systems now, to ensure Australians continue to have access to life saving and life improving treatments.

As HTA is a significant element in determining access to new treatments, it is vital we look at the impact of HTA as part of horizon scanning. Indeed, Australia's HTA methods and processes have not been significantly reformed since their commencement. The House of Representatives Standing Committee on Health, Aged Care and Sport *Parliamentary Inquiry into the approval processes for new drugs and novel medical technologies in Australia (Parliamentary Inquiry)* determined that reform is urgently needed to enable timely access to innovative medicines and vaccines.[7] The need for HTA reform has also been acknowledged by the Minister for Health and Aged Care.[8]

This year's Horizon Scanning Forum gathered a diverse range of decision makers and key stakeholders, including patient advocates, who called for urgent HTA reforms to prepare the system now and into the future.

> We are all in this together - industry, researchers, regulators and government – we need to work together to translate commercial advances in the lab and at the coalface.... we are working hard to get this right to support a really vibrant sector to put new tech and new medicines in reach for all Australian patients.
>
> – Opening address, The Hon. Ged Kearney MP

1.1 Novel vaccines to prevent infectious diseases

Technologies in the pipeline to prevent infectious diseases
Ms Jennifer Herz (session facilitator), Co-Founder & Director, Biointelect

Emerging communicable threats and Australia's preparedness
Prof Paul Kelly, Chief Medical Officer, Department of Health and Aged Care

Challenges and opportunities to implement novel technologies to prevent infectious diseases
Prof Paul Griffin, Director of Infectious Diseases at Mater Health Services Brisbane

Industry vaccines technology showcase presentations
Dr Krishan Thiru, Medical Director, Pfizer Australia
Dr Iris Depaz, Head of Medical Vaccines ANZ, Sanofi

Panel Q&A
Session speakers

This session included presentations and a panel discussion on the emerging infectious disease threats and Australia's preparedness; challenges and opportunities to implement novel technologies to prevent communicable diseases; and emerging vaccines technologies.

Importance of horizon scanning for novel vaccines

Infectious diseases continue to place significant burden on Australia's population. In 2023, infectious diseases (including COVID-19) were responsible for 2.5% of the total burden of disease in Australia, affecting an equivalent of 4.37 persons per thousand population.[9] Vaccines offer a compelling solution to both established and emerging health threats, through its mechanism of delivering an antigen to trigger the body's immune response, without causing the disease itself, resulting in immunity against one or several infectious diseases.

The rapid acceleration of vaccine development and the promising pipeline of new technologies emphasise the need for robust horizon scanning processes. Investing in early scientific advice and enhancing collaboration between stakeholders will be crucial for maximising the benefits of new research and ensuring timely and effective prevention strategies.

Australia's Chief Medical Officer, Professor Paul Kelly, noted in his presentation that horizon scanning for infectious diseases should encompass novel vaccines in development, as well as an analysis of emerging threats, such as surveillance of infectious diseases most likely to cause future pandemics.

Vaccines on the horizon

In recent years, the field of vaccines has experienced a significant transformation, largely driven by the challenges and innovations brought about by the COVID-19 pandemic. Historically, vaccine development took around 14 years, but advancements have now drastically reduced this timeline to just one or two years for some vaccines. The introduction of mRNA vaccines represents a breakthrough, highlighting the rapid evolution of vaccine technology and prompting a re-evaluation of future prospects in this field.

This session focused on emerging technologies and new tools for preventing infectious diseases beyond traditional vaccines. Innovations including DNA vaccines, which use genetically engineered DNA to trigger an immune response, are still under research, with trials for diseases like influenza and HIV. Combination vaccines, containing two or more antigens, can protect against multiple diseases or strains with a single shot. The DTaP vaccine is an example of a combination vaccine, protecting individuals from three distinct but serious diseases: diphtheria, tetanus, and pertussis. Vaccines against newly preventable diseases, such as respiratory syncytial virus (RSV), have also emerged from decades of scientific progress. Innovations in delivery technologies, like nasal sprays and skin patches, are expanding administration options making protection against diseases more accessible and user-friendly than ever before.

Jennifer Herz, co-founder and Director of Biointelect, revealed there are approximately 2,000 candidates in the global vaccine pipeline for infectious diseases, with the majority still in preclinical stages. Notably, 67% of these are industry-sponsored, contrasting with the academic focus on preclinical research in Australia. Recent data from the US Biotechnology Innovation Organization (BIO) shows the industry-sponsored vaccines clinical pipeline includes 249 candidates, many targeting viral pathogens, indicating a strong focus on viral diseases compared to bacterial or parasitic ones (Figure 2). This pipeline also includes novel vaccines for 31 infectious diseases for which there are currently no approved vaccines. There is also a diverse array of vaccine modalities in clinical stages, including mRNA, protein-based, and live attenuated vaccines.[10]

These developments underscore the need for horizon scanning to ensure systems are prepared for future advancements.

Figure 2: Global industry-sponsored clinical vaccine pipeline for infectious diseases

Pathogen Type	Phase I	Phase II	Phase III	BLA	Total
Non-CoV-2 RNA viruses	49	22	10	3	84
SARS-CoV-2 RNA virus	32	23	14	0	69
DNA viruses	14	14	6	0	34
Bacteria	12	20	11	1	44
Parasites	4	4	0	0	8
Multiple Pathogen Types	8	2	0	0	10
Total	**119**	**85**	**41**	**4**	**249**

BLA = Biologics Licence Application to US Federal Drug Administration

Source: Published with permission from the Biotechnology Innovation Organization (Bio)

mRNA vaccines

— Presenter: Dr Krishan Thiru, Country Medical Director, Pfizer Australia

The mRNA platform has the potential to provide combination respiratory vaccines that may provide a substantial additional public health benefit. Traditional vaccines work by giving a person either viral proteins or an inactivated or weakened version of a virus that triggers an immune response. mRNA vaccines do not contain viral material. Instead, these vaccines contain lipid nano-particles that surround a segment of mRNA, which provide cells with the instructions to make a certain viral protein, prompting an immune defense response.

One of the key features of the mRNA platform is the ability to quickly and efficiently scale production once the target protein sequence has been identified. The time from template DNA through to filtration and sterilization of a proposed mRNA sequence can be achieved faster than in traditional egg-based vaccines – paving the path for increasing scale of production and manufacturing to occur expediently.

The manufacturing of traditional, egg-based influenza vaccines is a complicated and lengthy process that requires the prediction of circulating influenza strains more than six months before respiratory virus season.[11] mRNA vaccine technology allows for more rapid vaccine production, which could enable viral strain selection closer to respiratory virus season.[12] This could increase the likelihood for the vaccine to match circulating strains more closely, which could potentially result in better protectivity and improved patient outcomes, subject to regulatory approval and clinical success.[13]

In terms of COVID-19, as the SARS-CoV-2 virus has continued to change, our ability to identify sequences causing disease to be included in a variant-adapted vaccine has been critical. However, the benefit of speed and scale that mRNA technology offers may have much broader applications.

Current vs future state of vaccines development and evaluation

— Presenter: Dr Iris Depaz, Head of Medical Vaccines ANZ, Sanofi

Changes occurring in vaccines development will impact how vaccines are assessed and valued. Innovation in research and development (R&D) using AI and machine learning, has improved strain selection and these can be combined with new cell, recombinant and mRNA vaccine platforms. This innovation will result in the ability to produce influenza vaccines which consistently deliver high effectiveness and optimal protection.

Innovations in influenza vaccine development will impact how we evaluate and value vaccines in the future in various ways, including:

- The way trials are conducted will be different, so the basis of the evaluation needs to reflect this change.
- Influenza vaccine effectiveness will be driven by the combination of the vaccine platform and the AI algorithm. As machine learning improves, effectiveness will continue to improve.
- We may need to transition from the current low value, commoditised view of influenza vaccines to support and invest in innovations in the space.

Figure 3. New ways to tackle existing challenges

Source: Dr I. Depaz presentation; Horizon Scanning Forum 2024

Implications for the health system and patient access

We are in a new era of infectious disease, characterised by outbreaks of emerging, re-emerging and endemic pathogens, and investment in preventing disease is critical to the health of people, our economy and the sustainability of our healthcare system. Australia needs to get ready now for upcoming vaccine breakthroughs by tackling the obstacles that delay vaccine access. This proactive approach will minimise the toll of infectious diseases on Australian's health, as well as on the healthcare system and the economy.

Valuing prevention

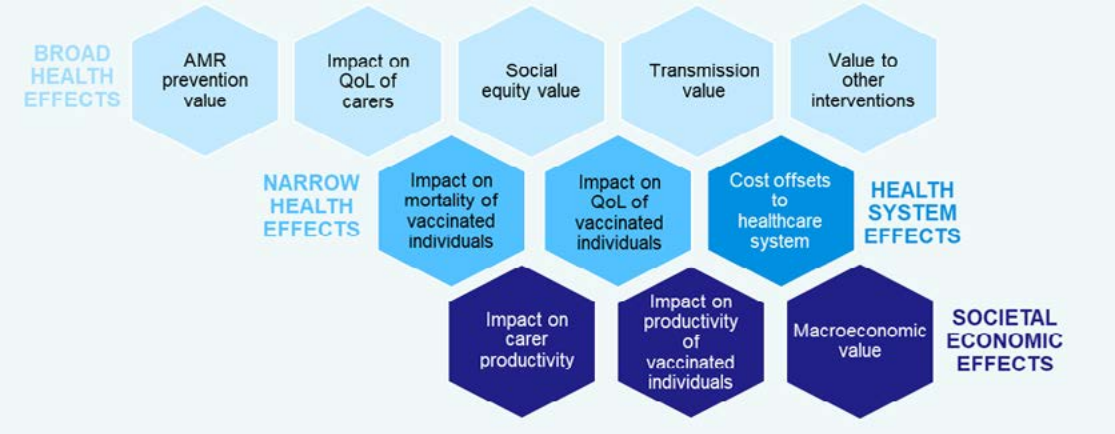
Investment in preventing disease must ensure that our regulatory and reimbursement processes are ready to efficiently evaluate and appropriately value innovative therapies, to enable timely access to breakthrough vaccines.

HTA discount rates reflect how health outcomes seen sooner are more valued than the health benefits that endure or accrue over a longer timeframe.[14] Many medicines, vaccines and treatments provide long-term health benefits. For example, a child receiving a polio vaccine will reap the benefits of that vaccine for the rest of their life. For treatments that have long-term or lifelong benefits, a discount rate is applied, which means the longer-term health benefits are not valued as highly. The PBAC set the base discount rate at 5% in 1990, the midpoint of the accepted discount rate range at the time of 3% to 8%.[15] Since that time, this discount rate hasn't changed, despite other Organization for Economic Cooperation and Development (OECD) nations (including Canada and England), recommending lower base discount rates - thus valuing higher the longer term benefits - to better fund future preventative and curative medicines, vaccines and treatments. If left unchanged, the current discount rate will risk significantly reducing patient access to cutting-edge vaccines. This will affect young people who stand to benefit the most from preventative medicines early in their life, as well as adult populations who are living longer but with poorer health.

The HTA Review Options Paper recommends more modelling of the impact where the discount rate is modified. Medicines Australia's position it that the discount rate must be lowered to 1.5% for medicines where benefits accrue over a longer time, in line with the international best practice and comparable countries. Further, a reduction in the discount rate should not be offset by changes to other variables such as the incremental cost-effectiveness ratio (ICER), otherwise there will be no net change to the value and hence no recognition of the longer-term outcomes and no change in the speed of patient access.

> "Australia's base discount rate was set at 5% in 1990 and hasn't been changed in more than 30 years."

Figure 4: Value of vaccination framework [21]



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Recognising the value of adult vaccination

While substantial progress has been made in childhood immunisation in Australia and globally, the value of adult immunisation programs is often overlooked. The burden of vaccine-preventable diseases is projected to rise due to an ageing population and emergence of novel infectious diseases, which highlights the importance of robust adult immunisation programs. Moreover, for infectious diseases such as shingles and pneumococcal disease, the incidence and severity of symptoms can increase with age, placing substantial burden on costly acute healthcare systems.

Expanding access to a broader adult population can generate more value and higher net cost savings for healthcare systems and society. A recent study across ten countries, including Australia, showed that adult immunisation programs present a great opportunity to help our societies age well and sustainably long into the future. Research has shown adult immunisation programs can deliver an excellent return on investment - up to 19 times the initial investment. [17]

The current relative lack of focus on adult vaccinations suggests there is a limited perspective on the benefits of vaccines. This is further demonstrated by economic evaluations for listing on Australia's National Immunisation Program (NIP), which explicitly consider only healthcare system related costs and outcomes. [18] This excludes important 'second order effects' of vaccines, such as workforce productivity and keeping the economy functioning – clear benefits derived through COVID-19 vaccines. This means the full benefit that vaccines deliver to society and the economy is not explicitly considered when making investment decisions under the current HTA framework. *The New Frontier Report* that resulted from the Parliamentary Inquiry into approval processes for new drugs and novel medical technologies in Australia in 2020, highlighted that the narrow focus of economic evaluations often hinders new medicines and medical technologies from fully showcasing their longer-term benefits to society. [19]

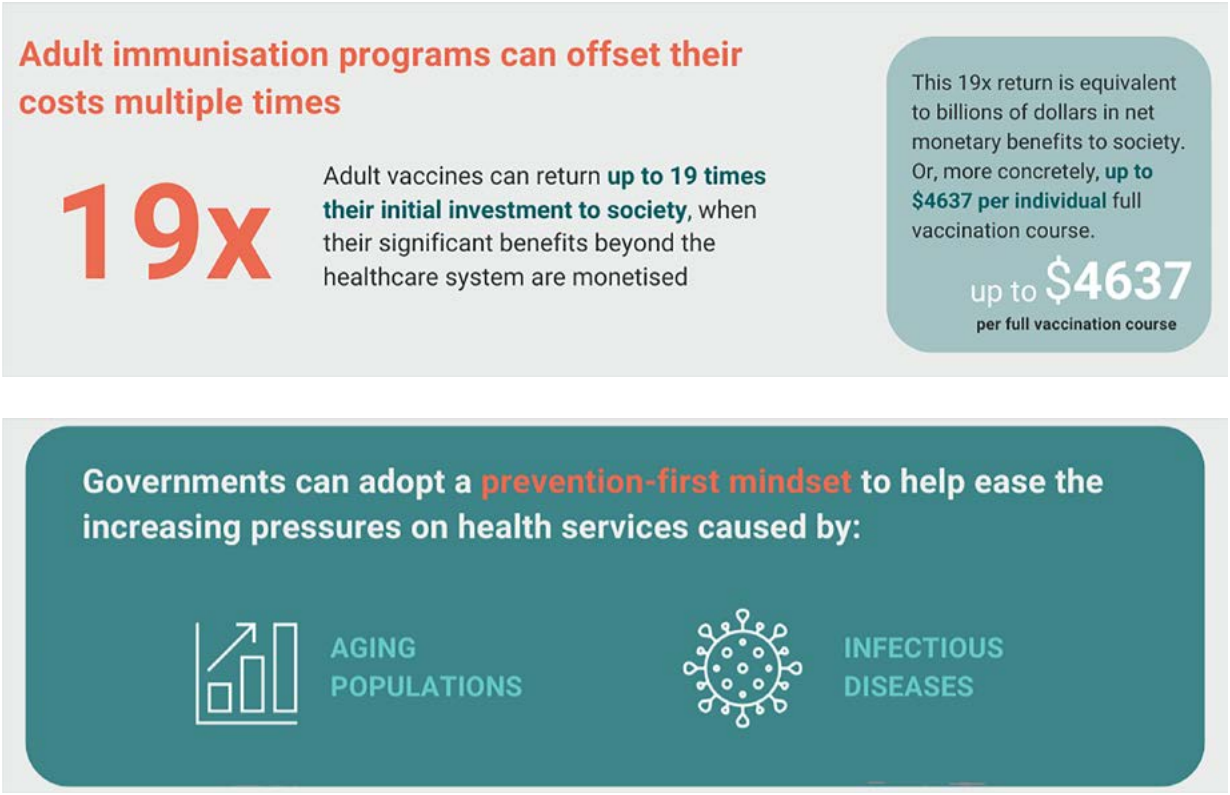
Explicit, published value frameworks that recognise these broader societal benefits, are already recommended and applied by expert committees and organisations such as the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), US Institute for Clinical and Economic Review (US ICER), and the UK National Institute for Health and Care Excellence (NICE). [20]

Encouragingly, the HTA Review Options Paper proposed development of an explicit qualitative framework, in consultation with a range of stakeholders.

Medicines Australia's response to the HTA Review Options Paper called for the framework to include elements such as:

- Wider societal benefits (e.g. non-patient outcomes).
- Patient and carer experience (e.g. improvements in convenience and adherence).
- Treatment choice (e.g. alternative mechanism of action or mode of administration)
- Equity (e.g. reduces geographical inequity if hospital admission not required).
- Real option value (e.g. life-extending treatments may allow for additional treatment options in the future).

Figure 5. Value of adult vaccinations [21]



Source: Published with permission from the Office of Health Economics (OHE).

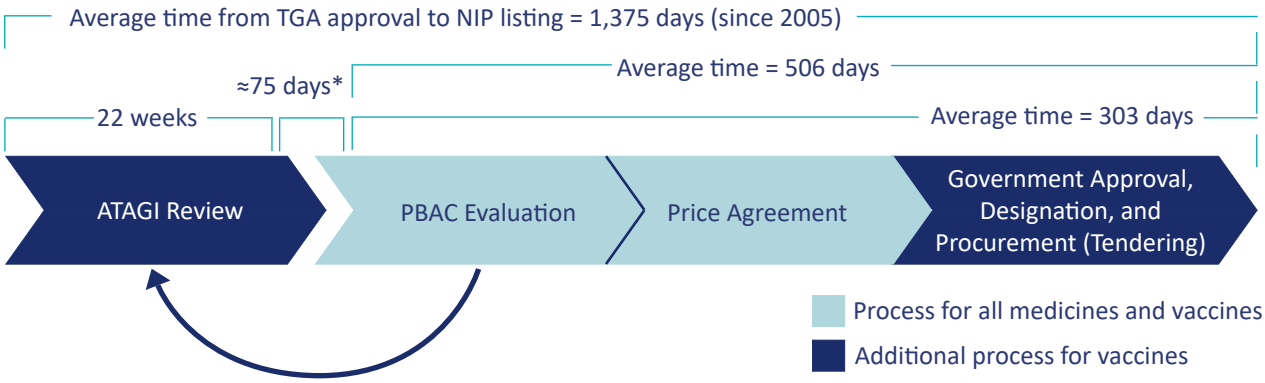
Streamline HTA processes

The process for securing funding for a vaccine under the NIP has become increasingly complex and costly. Vaccine companies must navigate four evaluation stages: TGA, the Australian Technical Advisory Group on Immunisation (ATAGI), the PBAC, and NIP tendering. Uniquely, Australia requires ATAGI, the National Immunisation Technical Advisory Group, and the PBAC to review vaccine inclusion recommendations. Another significant cause of patient access delays for vaccines is the drawn-out price negotiations to arrive at a price that routinely undervalues a vaccine. This highlights the complex, slow, and undervalued system for providing access to vaccines in Australia.

Streamlining these processes would reduce delays to access and deliver earlier benefits to Australians. These benefits extend to the wider community and healthcare system. The current time from registration to PBS listing of vaccines, an average time of 1,375 days or nearly four years, is unacceptable. [22]

The HTA Review has acknowledged the need to streamline the pathway for listing of a vaccine on the NIP. Medicines Australia supports a streamlined HTA pathway for vaccines where listing of vaccines is genuinely faster; where the pathways, decisions and processes are more transparent; and where greater value is placed on the preventative health benefits of vaccines.

Figure 6. Overview of the funding process for a vaccine on the NIP



* Time between final endorsed ATAGI advice, and next deadline for major submissions to PBAC

Vale Dr Iris Depaz PhD FTSE EMBA GCHEd

The Medicines Australia Board and team are deeply saddened by the passing of Dr Iris Depaz, a longstanding advocate and champion of the medicines, vaccine, and life sciences sector.

As Head of Medical Vaccines and Managing Director of the Translational Science Hub in Queensland at Sanofi, the industry has lost an intelligent, passionate and hands-on advocate for our sector. All who knew Iris understood and felt her unwavering commitment and her willingness to provide hands on advocacy for Australian medical innovation and better health for all Australians. Beyond this, Iris was well known for her warmth, care and authentic leadership.

The loss of Iris has been felt heavily by Medicines Australia and those who had the pleasure of working closely with her. We remember her commitment and engagement to the Horizon Scanning Forum, and thank Sanofi for their continued championing of her vision and legacy. Vale Iris.

1.2 Antimicrobial resistance and novel antimicrobials

Patient story
Mr Chris Bond OAM PLY, Captain of the Australian Steelers Wheelchair Rugby team

The AMR crisis
Mr Andrew Bowskill (session facilitator)
Director of Stakeholder Engagement for Queensland, MTPConnect. Co-chair Australian Antimicrobial Resistance Network (AAMRNet)

Antimicrobial Regulation and Reimbursement
Ms Renae Beardmore, Managing Director, Evohealth

AMR, the clinical experience, and Phage Therapy
Prof Jon Iredell, Senior Staff Specialist, Infectious Diseases & Microbiology, Westmead Hospital

Industry antimicrobial technology showcase presentation
Dr Scott Preiss, Medical Affairs Director, Vaccines, GSK

Session panel Q&A
Session speakers and Mr Mike Stephens (Director of Medicines Policy and Program at the National Aboriginal Community Controlled Health Organisation (NACCHO)

Importance of horizon scanning for novel antimicrobials

This session sought to showcase emerging novel antimicrobials and raise awareness among decision makers of what we stand to lose in the future if it we do not address the challenges of AMR today. AMR occurs when bacteria, viruses, fungi, and parasites stop responding to medicines. These medicines include antibiotics, antivirals, antifungals and antiparasitics and are collectively known as antimicrobials. Resistance of pathogens to antimicrobials make them ineffective, leading to infections that are harder or even impossible to treat. As a result, the risk of disease spread, severe illness, disability, and death increases.

The World Health Organisation (WHO) has identified AMR as one of the top global public health threats. It is estimated that AMR is attributed to 1.27 million deaths and associated with 4.95 million deaths worldwide in 2019. [23] The scale of the AMR problem is so significant that it is projected to cause more deaths than cancer by 2050. [24]

Antimicrobials are crucial to modern medicine, significantly extending human lifespan by over 20 years. They combat life-threatening infections and support various medical treatments, including cancer therapies, organ transplants, and safer childbirth. Effective antimicrobials are essential for managing severe infections like sepsis, which claimed 8,500 lives in 2017, and for successful transplant outcomes and cancer treatment, where infections are a leading cause of death.

This issue is exacerbated by a crisis of patient access to new antimicrobials. Many countries, including high-income countries like Australia, suffer from limited access to the latest antibiotics. There is also a lack of investment into the research and development and commercialisation of new antimicrobials, which is reflected in a dwindling

pipeline of new antimicrobials. This is in stark contrast to investment in new cancer therapies. In 2020, $7 billion was raised for cancer treatments compared to just $160 million for antimicrobials.[25]

As the effectiveness of last-resort antimicrobials is compromised, the risks of infections that cannot be treated increases. Projections by the OECD indicate an anticipated two-fold surge in resistance to last-resort antimicrobials by 2035, compared to 2005 levels, underscoring the urgent need for action against AMR, including addressing the pipeline and access crisis for antimicrobials. [26]

> Only 19 novel antimicrobials have been registered for use in the EU and/ or the US since 2011. Of those, only 3 are registered in Australia; none are reimbursed through the PBS.
>
> – Session facilitator, Andrew Bowskill

Despite their importance, AMR continues to pose a major threat to public health. Of particular concern is the lack of novel antimicrobials in development. This underinvestment is coupled with a crisis of access and a policy framework that undervalues antimicrobials. The existing reimbursement models are linked to sales volumes, which conflict with the necessary stewardship practices that limit antimicrobial use to preserve their effectiveness. This misalignment discourages the development and market introduction of new antimicrobials.

The crisis is not only a problem of investment but also one of policy and research. The return on investment for antimicrobials is poor compared to other treatments, leading to fewer resources and researchers focus on this field. The pipeline of new antimicrobials is insufficient to meet the growing rates of resistance. To address these issues, urgent action is needed. International bodies like the G7, G20, the Asia-Pacific Economic Cooperation (APEC), and the WHO are calling for enhanced measures. The September 2024 United Nations (UN) General Assembly High-Level meeting on AMR aims to drive substantial actions. In Australia, there's increasing recognition of the need for reform. Efforts are underway to translate this awareness into initiatives, including improving access and fostering innovation.

The Australian Antimicrobial Resistance Network (AAMRNet) has identified areas for action: enhancing the research environment, investing in a pilot subscription fund for new antimicrobials, and supporting regional efforts in the Western Pacific. Addressing AMR effectively will require both global and local efforts to ensure antimicrobials continue to play their critical role in modern medicine.

Presentations in the AMR session emphasised that HTA policies and processes are a potential barrier to the introduction of novel antimicrobials in Australia. Despite rising levels of AMR, novel antimicrobials in Australia are often considered to be undervalued due to the availability of low-cost generics and the lowest cost comparator reference pricing policy, which in turn impedes a pharmaceutical company's ability to realise a commercial return.

Industry, along with other leading AMR advocates stress the urgency of implementing both push and pull incentives to quickly deliver innovative antimicrobials to patients. This proactive strategy is essential for advancing healthcare and addressing AMR. Push incentives can reduce early-stage R&D costs and risks (e.g. through research grants and tax incentives), while pull incentives ensure successful commercialisation and patient access via conditions for improved profitability, thus attracting investors. [27]

In his presentation, Andrew Bowskill shared the stark statistic that only 19 novel antimicrobials have been registered for use in the EU and / or the US since 2011. Of those, only 3 are registered in Australia. [28] None are reimbursed through the PBS.

AMR: A Paralympian's experience

— Presenter: Chris Bond, Captain of the Australian wheelchair rugby team

"As a lay person you don't think about the complexities of antimicrobial resistance, and you think there will always be an abundance of antibiotics to fix you... It is easy to be disconnected to the issues, so my challenge to you is to think about what if it was you."

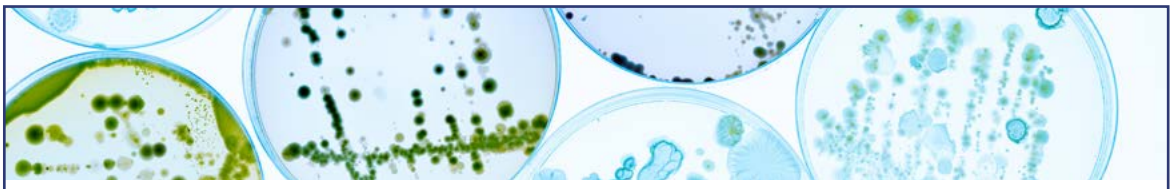
Chris Bond was a fit and healthy 18 year old when he began experiencing stomach pain. After ignoring the symptoms for two weeks, the pain became so severe he went to the hospital emergency department where he was diagnosed with a severe bacterial infection.

Within hours, Chris underwent emergency surgery to save his life. In addition to a necrotising fasciitis infection, which was attacking his body, Chris was also diagnosed with acute promyelocytic leukaemia. Chris was put into an induced coma for three days after surgery. Over the next month while he was in the hospital's intensive care unit (ICU), his extremities turned gangrenous due to lack of oxygen and his left hand, right fingers and both legs below the knees had to be amputated.

Chris spent more than 10 months in hospital recovering from the infection before he was able to start cancer treatment that continued for three years. The cancer treatment made Chris more susceptible to infections and he contracted many further infections while in hospital. It became increasingly difficult for doctors to treat these infections as Chris developed resistance to many of the antimicrobials available.

Determined not to be defined by his disability and to achieve his lifelong goal of representing Australia in sport, Chris began playing wheelchair rugby and quickly progressed to international level. He has represented Australia at three Paralympic Games and will Captain the team at the 2024 Games in France.

After everything Chris has overcome, his biggest fear is a world where antimicrobials are no longer effective.



Panel discussion on AMR

— Presenter: Mike Stephens, Director of Medicines Policy and Programs at the National Aboriginal Community Controlled Health Organisation (NACCHO)

AMR is a critical issue facing Aboriginal and Torres Strait Islander communities. Antimicrobials are the most prescribed medicine in remote Australian Aboriginal and Torres Strait Islander communities. This high demand for prescription medicines is needed to treat the common, serious infections that are well reported in these communities due to the high burden of disease such as renal disease requiring dialysis, cancer, infectious diseases such as rheumatic heart disease, syphilis and tuberculosis.

Financial incentives for development of novel antimicrobials are important to meet the high unmet clinical needs of Aboriginal and Torres Strait Islander communities. Solutions to address AMR for Aboriginal and Torres Strait Islander communities should also include self-governance and determination.

Andrew Bowskill

Director of Stakeholder Engagement for Queensland, MTPConnect. Co-chair Australian Antimicrobial Resistance Network (AAMRNet)

Renae Beardmore

Managing Director, Evohealth

Prof Jon Iredell

Senior Staff Specialist, Infectious Diseases & Microbiology, Westmead Hospital

Dr Scott Preiss

Medical Affairs Director - Vaccines GSK

Mike Stephens

Director of Medicines Policy and Program, National Aboriginal Community Controlled Health Organisation (NACCHO)

Antimicrobials on the horizon

The research and development of novel antimicrobials is an important component of the 'One Health Approach', which recognises that the health of humans, animals, and the wider environment are inherently linked and interdependent. Interventions to prevent, detect and respond to AMR must be multifaceted and involve collaboration across human, animal and environmental health sectors, to achieve sustainable and effective results.

AMR: An industry view

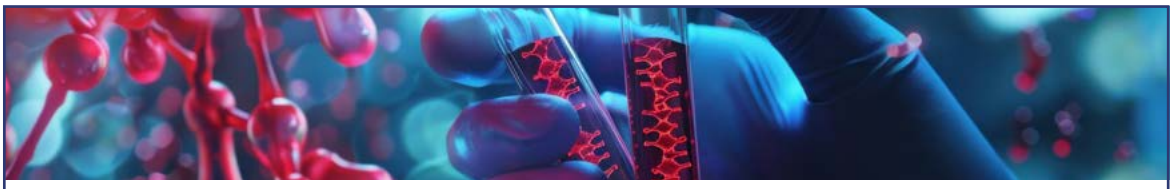
— Presenter: Dr Scott Preiss, Medical Affairs Director of Vaccines, GSK

GSK is recognised by the Access to Medicines Foundation as having the strongest AMR pipeline in industry,[29] including several vaccines and four first-in-class antimicrobials in different stages of development. One of these is a new first in class triazaacenaphthylene antibiotic for treatment of uncomplicated urinary tract infections (UTIs) and gonorrhoea. It has undergone clinical trials in Australia and targets E.coli. – a WHO critical priority pathogen. The antibiotic has a novel mode of action which blocks two key enzymes involved in bacterial replication.

A new reimbursement model which delinks the value of an antimicrobial from the volume used in the health system is essential to enable companies like GSK to launch novel antimicrobials in Australia.

Beyond developing new antimicrobials, GSK has been generating and disseminating surveillance data for almost 25 years through its Survey of Antibiotic Resistance (SOAR). It is now running in more than 30 countries in the Middle East, Africa, Commonwealth of Independent States, Latin America, Asia, China and Eastern Europe. The SOAR study is repeated every 2-3 years to identify resistance trends in different countries.

In 2016, a specific educational Global SOAR Forum Meeting was held during World Antibiotics Awareness Week to disseminate the latest SOAR data from 17 countries, build healthcare professionals' knowledge of local susceptibility factors and outline how this knowledge could be put into practice to help them choose and prescribe antibiotics appropriately.



Critical infection and AMR

— Presenter: Professor Jon Iredell.
Conjoint Professor of Medicine and Microbiology, Sydney Medical School and Sydney Infectious Diseases Institute.
Director of Centre for Infectious Diseases and Microbiology, The Westmead Institute for Medical Research.
Senior Pathologist, NSW Pathology and Institute of Clinical Pathology and Medical Research.

Prof Iredell is a physician and microbiologist based at Westmead Hospital and the University of Sydney. His research group works on infections in the critically ill and AMR. Recent work in the laboratory has focused on new solutions for antimicrobial resistant infections, including plasmid displacement approaches and bacteriophage therapy.

Prof Iredell shared insights into the impacts of AMR from a clinical perspective. He is optimistic about the opportunities for antimicrobials given antimicrobial stewardship, innovations such bacteriophages (natural predators that control bacteria), and advances in gene therapy in antimicrobial resistant bacteria.

To balance the risk and reward to enable improved access to novel antimicrobials in Australia, Prof Iredell called on governments to:

- Take control – proactive is cheaper and better than reactive.
- Embrace innovation – agile regulatory environments.
- Consider safety nets to accommodate risk, such as subscription reimbursement models.

Implications for the health system and patient access

Pull incentives: Pilot a subscription model in Australia

MTP Connect's second Fighting Superbugs Report recommended Australia implement a pilot fully de-linked subscription reimbursement model for antimicrobials to improve access and help address the antimicrobial market failures, drawing on the lessons from international experience.[30] Novel reimbursement models are not new in Australia's healthcare history, having been previously adopted for snake anti-venom and Hepatitis C. Subscription models are based on a minimum supply of a novel antimicrobial being made available for a fixed annual price. It is different from the current payment model, where revenue is generated based on the quantity of antimicrobials purchased within a health system.

> "The precedent is there. We don't need to re-invent the wheel. [Mechanisms] are already in place to make this happen"
>
> – Session presenter, Renae Beardmore, Managing Director, EVOHEALTH

Pull incentives: market protections and accelerated pathways

The New Frontier Report identified data exclusivity provisions in Australia as a potential barrier to access to novel drugs including antimicrobials. The report called for the extension of the data exclusivity period in Australia from five to ten years for novel drugs and vaccines.

Existing TGA accelerated pathways could also be better used and coordinated to ensure more novel antimicrobials are appropriately expedited through regulatory approval processes. This would shorten review registration timeframes, potentially reducing the time to market, thus reducing the cost, effort, risk and duration of R&D for novel antimicrobials.

HTA Review options: antimicrobials

The HTA Review Options Paper suggested incentives to promote the development of products that address AMR:

1. HTA fee exemptions for products that address AMR.
2. Scope potential changes to HTA policy and methods related to products that address AMR.
3. Workshop and test multiple payment and incentive models as part of designing a flexible reimbursement policy for purchasing of antimicrobial products.

Medicines Australia agrees that implementing payment and incentive models for novel antimicrobials is crucial in the fight against AMR. We support a subscription model as described by MTPConnect and others. Several workshops have been held in recent years to scope approaches and there are several successful international pilots for subscription models that delink reimbursement from volume that could serve as frameworks for an Australian model. Workshops should be reserved to finalise details of a delinked model rather than further discuss options.

1.3 Cell and gene therapies

Cell and gene therapies – call for strategic coordination
Dr Marguerite Evans-Galea AM (session facilitator)
Director, Australia's Cell and Gene Catalyst

Cell and gene therapies – opportunities on the horizon
Prof John Rasko AO
Head of Department, Cell & Molecular Therapies, Royal Prince Alfred Hospital

Industry cell and gene therapy showcase presentations:

Chimeric Antigen Receptor (CAR) T therapy
A/Prof Philip Thompson, Peter MacCallum Cancer Centre

Barriers to patient access to cell and gene therapies
Mr Warwick Shaw, Market Access, Johnson and Johnson Innovative Medicine

CRISPR/ Cas9 gene editing therapy
Mr Quentin Bracquart, Principal, IQVIA Management Consulting

Session panel Q&A
Session speakers and Ms Agnes Nsofwa, Executive Director, Australian Sickle Cell Advocacy Inc, and Ms Katrina Lapham, Director Strategic Market Access and Policy, Biointelect

Importance of horizon scanning for CGTs

The scientific community is experiencing a boom in cell and gene therapies (CGTs). These therapies are complex health interventions, involving advanced biochemical techniques that target a patient's own immune cells or genes to deliver long-lasting therapeutic, or potentially curative benefits.

Cell therapies involve the transfer of live healthy cells into a patient using either their own cells, which have been modified in a laboratory or cells from a donor, to alleviate or potentially cure a disease. Gene therapies involve using a vehicle (e.g viral or bacterial vector) to deliver the correct genetic information to recode an abnormal cell to produce the correct proteins or protein levels.

This session demonstrated the transformative nature of CGTs by their ability to treat and potentially cure a range of health conditions such as some cancers, rare genetic disorders, and chronic diseases.

It may be the only option in rare genetic diseases, and it is particularly relevant to diseases caused by a single genetic defect. Rare diseases represent a significant unmet need with approximately 7,000 known rare diseases worldwide,[31] 80% having a genetic origin, and treatments only available for less than 5% of these diseases.

CGT on the horizon

Dr Marguerite Evans-Galea revealed that an avalanche of cell and gene therapies is coming, partly thanks to orphan drug designations and priority review pathways that can fast track therapeutics from bench to bedside, the wealth of knowledge gained from the Human Genome Project, and advances in genomics and improved DNA sequencing capabilities and diagnostic assays. This presents Australia with an immense opportunity.

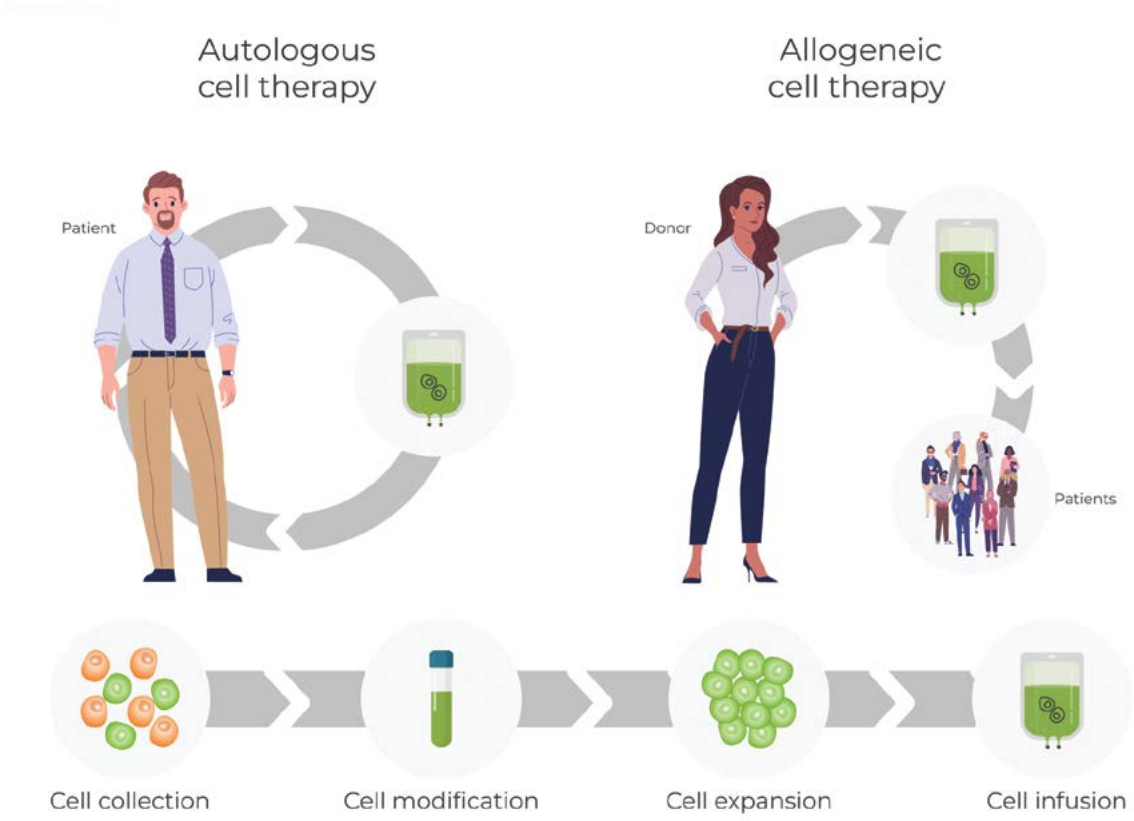
As of 2020, there were 641 cell and 536 gene developers worldwide working on CGTs. There are more than 2,000 human clinical trials involving CGTs reported worldwide and the United States Food and Drug Administration (FDA) has projected that by 2025, they will be appraising 10 to 20 CGT products per year.[32]

One such gene therapy, Chimeric Antigen Receptor T-cell therapy (CAR-T) is a form of personalised and precision medicine, where T-cells are reprogrammed to target and kill cancer cells. It is a form of immunotherapy has revolutionised the treatment of various blood cancers like acute lymphoblastic leukemia, lymphoma and myeloma, as well as haemophilia.

T-cells are collected from a patient (autologous) or from a donor (allogeneic). The cells are modified outside the body, expanded and then infused into the patient. CAR T-cell therapies that have been approved to date are autologous and allogeneic therapies are still in clinical trials.

> There are more than 2,000 human clinical trials involving CGTs reported worldwide.

Figure 7. Autologous and Allogeneic CAR-T cell treatment process [33]



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Using genes as medicines

— Presenter: Professor John Rasko AO
Head of Department, Cell & Molecular Therapies, Royal Prince Alfred Hospital, Sydney Local Health District (SLHD). Deputy Director & Head, Gene and Stem Cell Therapy Program, Centenary Institute. Professor, Faculty of Medicine & Health, The University of Sydney.

CGTs offer transformative potential for treating and curing diseases. Building on the work of German pathologist Rudolph Virchow, who noted that a single cell can divide into many, leading to the production of millions of red blood cells each second, we now understand that our genetic material, DNA, plays a crucial role in this process. DNA contains the genetic information passed from one generation to the next. The concept behind using CGTs as medicine involves introducing new genetic material into cells to reprogram them, enabling them to perform functions they couldn't previously do due to genetic diseases.

Gene modification can be achieved through two primary methods: *in vivo* and *ex vivo*. *In vivo* gene therapy involves injecting genes directly into the body, potentially targeting tumours or other tissues. *Ex vivo* gene therapy involves removing a patient's cells, modifying them outside the body, and then reintroducing them to the patient. Both methods have been successfully employed in various clinical settings.

A notable advancement in gene therapy is in cancer treatment, where understanding the genetic basis of cancer has led to new therapeutic approaches. CAR T-cell therapy, for example, reprograms a patient's immune cells to specifically target and attack cancer cells. This personalised and precise approach has revolutionised the treatment of certain blood cancers and showcases the potential of gene-based therapies.

Similarly, gene therapy has made significant strides in treating haemophilia. By providing a one-time treatment that allows patients to produce necessary clotting factors themselves, gene therapy reduces reliance on ongoing treatments and avoids risks associated with blood product transfusions. Over the past 20 years, advancements in this field have led to approved therapies for both haemophilia A and B in major markets.

Looking forward, the field of molecular medicine continues to evolve. The development of induced pluripotent stem cells (iPSCs) has opened new possibilities for regenerative medicine. For example, Australian researchers have pioneered clinical trials using reprogrammed iPSCs to treat complications related to bone marrow transplantation. These innovations, published in prestigious journals, underscore the growing potential of these technologies.

The future of gene and cell therapy is promising. The ability to modify genetic material and reprogram cells offers the potential to address a wide range of diseases. While ethical, regulatory, and economic considerations are critical, the progress in this field suggests that gene and cell technologies could one day provide cures for many currently incurable conditions, offering hope for a brighter future in medicine.

CRISPR/Cas9 gene editing: A new pace of innovation in CGT

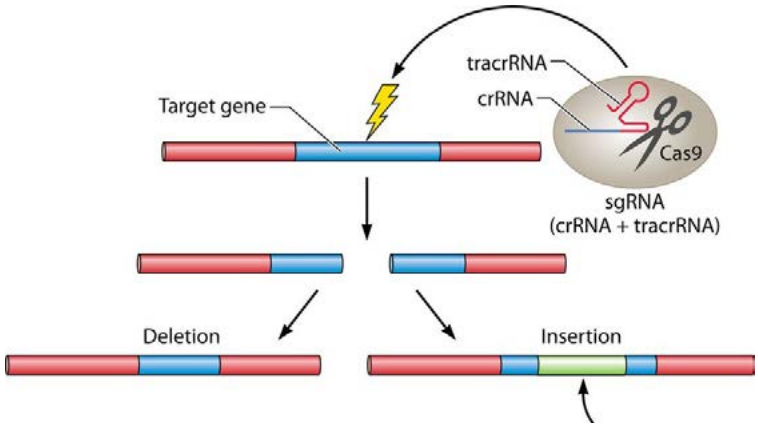
— Presenter: Quentin Bracquart, Principal in the Management Consulting team in IQVIA Australia and New Zealand, and Head of Payer, Provider and Government Services.

The novel CRISPR gene editing technology allows precise changes to be made to DNA. The translation from laboratory to clinic has been incredibly fast, taking approximately 11 years from discovery to registration in the USA. There are currently 46 active clinical trials using CRISPR systems, the majority in haematology and oncology.

CRISPR gene editing technology holds the potential to cure patients with, in particular, monogenic diseases. In clinical trials, CRISPR gene editing therapy for patients with sickle cell disease has demonstrated that close to 95% were free from severe episodes up to 24 months after the gene therapy. For patients with transfusion dependent beta thalassemia, 93% of patients were transfusion free for at least one year.

In a case study of a gene editing trial involving a private site in Australia, under the current National Healthcare Reform Agreement (NHRA) block funding system, this hospital would not be able to receive public funding for providing the therapy once it has received regulatory and HTA approval, despite safety accreditations for delivery obtained by major manufacturers. This is a disincentive for private hospital sites to conduct CGT trials and this may contribute to Australia becoming less competitive in the global clinical trials space in the longer term. In addition, with each new therapy increasing demand for hospital beds, clinical resources, infrastructure and clinical and administrative staff, private sites may play a key role in alleviating capacity constraints.

Figure 8. Genome editing by CRISPR-Cas9



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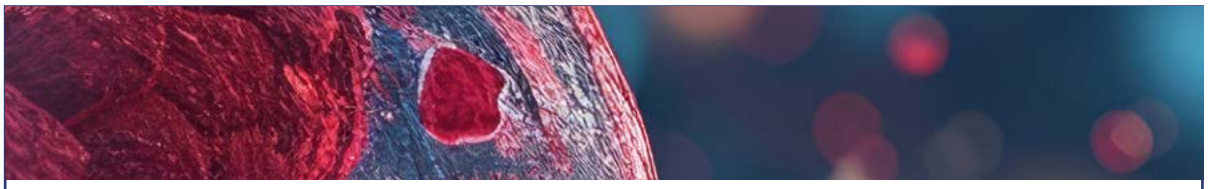


Chimeric Antigen Receptor (CAR) T-Cell Therapies - current practice and potential innovations

— Associate Professor Philip Thompson, University of Melbourne, Peter MacCallum Cancer Centre

Current Practice

There are 4 CAR T-cell products registered in Australia for 7 indications. Of the 4 registered CAR-T cell products, 3 are funded for 4 indications, including acute lymphoblastic leukemia (ALL), diffuse large B-cell lymphoma (DLBCL), large B-cell lymphoma (LBCL) and mantle cell lymphoma (MCL).

Although the 3 CAR T-cell products have been funded in Australia since August 2019, a significant access gap exists, delaying clinical use by 9 to 30 months due to time required for HTA Review and state government agreements. It is critical to reduce this access gap as these treatments are for patients with relapsed refractory cancers and poor prognoses.

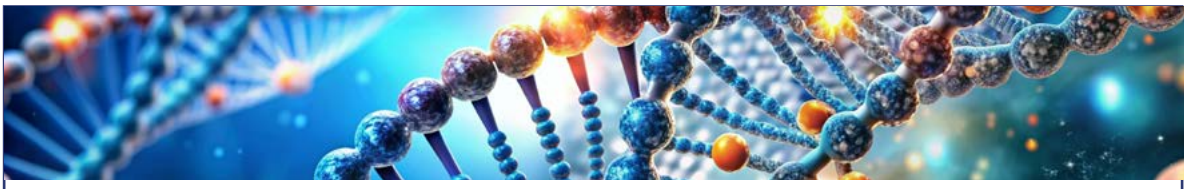
CAR-T cell therapy clinical trials continue to show promising results. For diffuse large B-cell lymphoma, survival rates improved dramatically with over 40% of patients alive at five years, compared to a near 100% fatality rate without the therapy.

Between January 2020 and October 2023, the Peter MacCallum Cancer Centre administered CAR -T- cell therapy to 130 patients - about one-third of Australia's total infusions. Referrals come mostly from outside the centre, with patients seen within three days. After confirming eligibility, the T cells are harvested and sent to the U.S. for processing, which takes 4 to 6 weeks. Rapid disease progression can make it challenging to keep patients stable during this period, leading to an average 11% order cancellation rate over this time period.

However, the cancellation rate decreased from 20% in 2020 to 5% in 2023 due to better bridging therapies and patient selection, but further work is needed to address the remaining gaps.

Potential innovations

Allogeneic (donor-derived) cell therapies are currently being evaluated in clinical trials. This technology would provide immediate availability of treatment so that CAR T-cell therapy could be an option for patients who are progressing quickly and cannot be sustained on bridging therapy while waiting for manufacturing. Additionally, obtaining the source material from healthy donors may give an improved yield and more consistent product. Key remaining challenges for allogeneic CAR T-cells are graft-vs-host disease and host allorejection, which might be overcome by genetic modifications of the T-cells or by using alternative cell sources/subpopulations for allogeneic CAR cell production. Another emerging CAR technology is the modification of natural killer cells derived from umbilical cord blood. Allogeneic CAR cells are an active area of research, with at least 80 ongoing studies worldwide, and 10 trials with Australian sites.[34,35]



A cure for sickle cell disease

— Presenter: Agnes Nsofwa, Founder and Executive Director of Australian Sickle Cell Advocacy (ASCA)

Agnes' daughter, Mapalo-Joy, was diagnosed with sickle cell disease at 14 months of age and became the first child at the Royal Children's Hospital to receive a bone marrow transplant for sickle cell disease. Mapalo-Joy's condition was missed during early pregnancy. After her birth, doctors failed to diagnose her sickle cell disease, which led to numerous hospital visits and misdiagnoses. Agnes consistently raised concerns about her child's health, but it wasn't until she was 14 months old that doctors conducted a full blood check.

At the time, there was only one medication available in Australia to treat sickle cell disease, which was originally used for cancer treatment. Uncomfortable with this option, Agnes researched alternative treatments and discovered bone marrow transplants may offer a potential cure. After seeing an interview on TV with a doctor who cured a boy with aplastic anaemia, Agnes reached out. The doctor agreed to take the case on, and Agnes's family moved to Melbourne to access treatment at the Royal Children's Hospital. In 2019, Mapalo-Joy had a bone marrow transplant, with her sister Cecilia being the donor, which cured her of the disease.

While bone marrow transplant was a life saving cure for Mapalo-Joy, the treatment is not accessible for all patients due to a range of barriers, including availability of a suitable donor and risks of complications for some patients.

Agnes continues to advocate for the sick cell disease community in the hope of improving access to new and effective treatments for the disease.

L-R: Preston Nsofwa (father), Mapalo-Joy and Agnes Nsofwa

L-R: Mapalo-Joy and her sister Cecilia

Barriers to CGTs for Australian patients

— Presenter: Warwick Shaw, Market Access, Johnson&Johnson Innovative Medicine

CGTs are increasingly becoming standard treatments, with real-world outcomes surpassing those seen in clinical trials. However, the pipeline of these therapies highlights that there is still much to be done to ensure broader accessibility and better integration into healthcare systems.

In Australia, current reimbursed CGTs address specific conditions such as certain blood cancers, inherited retinal diseases, and spinal muscular atrophy. These therapies are available to only small patient populations compared to other countries, which offer a wider range of treatments for various diseases. Some of these therapies can significantly improve patients' quality of life, especially where no other treatment options exist.

A significant barrier is the travel distance required for patients to access these therapies. For example, half of the CAR T-cell therapy patients have had to travel over 100 kilometres to receive treatment, often passing by closer, potentially qualified hospitals. In some cases, patients need to travel outside their state or territory, which adds significant stress and risk to their already vulnerable condition.

Currently funded CGTs are only available at sites approved by the local state or territory Department of Health. To date, these therapies are only available in a handful of public metropolitan tertiary centres. Due to NHRA funding conditions, these therapies cannot be accessed in private hospitals. Also, access to the currently funded CGT therapies is unavailable for patients within their home state or territory, if they reside in South Australia (SA), Tasmania (TAS), Northern Territory (NT), and ACT. The lack of public hospital activity-based funding codes and service codes further hampers equitable access to these treatments as they become standard of care for many diseases.

To capitalise on the transformative opportunities of CGTs, Medicines Australia and others have called for the following reforms:

1. **Accelerate equitable access**
    - Remove the gap between access to medicines as soon as possible after TGA registration.
    - Establish the Codes for efficient and equitable access by Public and Private Hospitals.
2. **Federal funding**
    - Establish a single federal funding source for the 'product costs' of CGTs.
3. **Recognise the value of innovation**
    - Give greater consideration for the unique health technology aspects of CGTs (such as one-off treatment, deep remissions and curative potential, reduced ongoing service utilisation and patient/carer quality of life).
4. **Standardise delivery**
    - Streamline and, where appropriate, standardise the clinical delivery of CGTs.

Figure 9. Access to CAR-T cell therapy by residential location

19% of patients travel out of their home State/Territory to access CAR T-cell therapy

Residence	NSW	QLD	VIC	WA	Total
ACT	5	1	1		7
NSW	127	3	13		143
NT	1	3	3		7
QLD	1	43	1		45
SA	1	3	15	1	20
TAS		2	6		8
VIC			108		108
WA	2		11	26	39
Total	**137**	**55**	**125**	**27**	**377**

Peter Mac data on patient State of usual residence	N (%)
Victoria	102 (70%)
Interstate	43 (30%)

Source: Published with permission: Warwick Shaw presentation from Horizon Scanning Forum 2024

Implications for the health system

While CGTs are transforming treatment regimes, they pose significant challenges to our healthcare system because they are not specifically a medicine, device or a service and can be a combination of each, and therefore do not fit neatly into current regulatory and reimbursement frameworks.

Regulation of CGTs falls under the remit of the TGA and the Office of Gene Technology Regulator (if the therapy involves gene modification). Once approved by the TGA for listing on the ARTG, CGTs can be assessed for clinical and cost-effectiveness, by either the Medical Services Advisory Committee (MSAC) or the PBAC. While the PBAC generally evaluates reimbursement of pharmaceuticals and MSAC for healthcare services, how a CGT is administered to a patient leads to different HTA pathways. For example, as with CAR-T, if genetic modification of patient cells happens outside of the body ('*ex vivo*') before being transferred back into the body, this is classified as a Class 4 biological. This distinction renders CAR-T unsuitable for PBAC consideration. Conversely, if a gene product is directly transferred into cells in a patient's body to make an '*in vivo*' change, it is classified as a prescription medicine and can be evaluated by the PBAC.

Australia has two main funding pathways for these therapies. One pathway includes therapies on the PBS, offering full federal funding and the possibility of delivery in qualified public hospitals. The other pathway falls under the NHRA, which requires a 50/50 federal and state funding split, which limits delivery to selected public hospitals, and mandates inpatient treatment. This NHRA structure is designed to enhance collaboration between federal and state governments but has proven challenging, especially given the high cost and complexity of therapies like CAR T-cell treatments.

With the growing number of CGT products in the global pipeline, there needs to be significant change in how care is delivered in Australia.

HTA Review options: CGT

The HTA Review Options Paper proposes government collaboration in HTA for health technologies that are jointly funded by the federal and state and territory governments. In contrast, Medicines Australia advocates for a streamlined approach to accessing CGTs through full federal funding, while acknowledging the ongoing significance of cooperative efforts with state and territory governments for these treatments.[50]

Medicines Australia, however, endorses the proposal in the HTA Review Options Paper to streamline and align HTA pathways for drugs for ultra-rare diseases, provided the intent of the Life Saving Drug Program (LSDP) to fund these medicines remains. As such, it is essential to recognise that these drugs are unlikely to be cost-effective using the same HTA principles as are applied to other medicines. There is limited data for ultra-rare diseases to meet the usual standards of comparative effectiveness and cost-effectiveness expected in HTAs. A different approach is needed, one that considers the unique characteristics of the specific diseases and proposed treatment.

Cell and Gene Therapies panel discussion

1.4 Digital health

Industry digital health showcase presentation: The Use of AI-driven in vitro diagnostic (IVD) tools
Dr Diana Zhang, Founder and CEO, Preview Health
Oona Reardon, Director, Pulse Economics Consulting

The Transformative Potential of Digital Health
Kim Smyth (session facilitator), General Manager, Investment, AndHealth

Panel Q&A
Session speakers and Olivia Nassaris, CEO Parkinson's Australia, and Dean Whiting, CEO Pathology Technology Australia (PTA)

Importance of horizon scanning for digital health

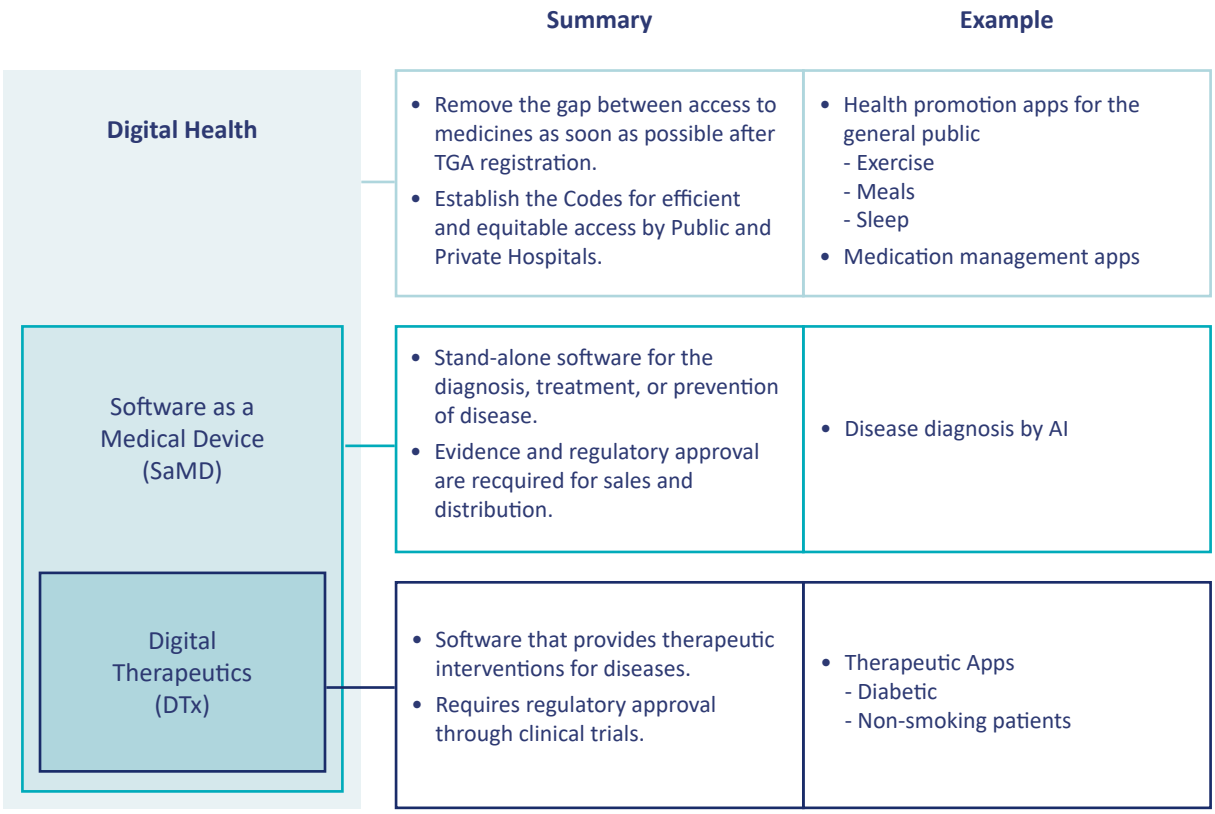
According to the WHO, digital health is "the field of knowledge and practice associated with the development and use of digital technologies to improve health".[38]

Digital health is being recognised globally as a key solution to the challenges posed by rising healthcare costs and shortages in human resources. Healthcare pressures are largely driven by increasing rates of chronic and complex disease and the rapid ageing of the population. The growth in digital health is supported by the growing technological infrastructure, including advancements in wearable technology, AI, machine learning, and other related technologies. These innovations are helping to meet the increasing demands on healthcare systems by improving efficiency and enabling more personalised care.[52]

Digital health encompasses far more than just electronic health records; it also includes mobile health (mHealth), health information technology (IT), wearable devices, telehealth, telemedicine, Software as a medical device (SaMD), digital therapeutics (DTx) and personalised medicine (Figure 10). This digital transformation in healthcare is driving the development of more tailored treatment options, with real-time data collection and analysis playing a crucial role. By leveraging these technologies, healthcare providers can personalise treatments to better suit individual patients, leading to potentially improved health outcomes.

L-R: Oona Reardon, Dr Diana Zhang, Tham Vo, Kim Smyth, Olivia Nassaris, Dean Whiting, Con Tablan

Figure 10. Types of digital health [39]



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Digital health on the horizon

Digital health is revolutionising the global pharmaceutical industry and healthcare more generally, using AI, big data analytics and machine learning in the development of biotherapeutic products, pharmaceuticals and vaccines. The use of AI and machine learning accelerates the discovery phase, enabling rapid analysis of massive datasets to identify potential treatment candidates, optimise experimental designs, and predict the success of these compounds. This could significantly reduce the time associated with drug development.

The digital therapeutics (DTx) market is projected to grow significantly, from $6.68 billion USD in 2023 to $25.24 billion USD by 2030, with a compound annual growth rate (CAGR) of 20.9%.[40] This rapid growth is driven by the increasing number of patients with chronic diseases and rising investments in DTx. The market faces challenges such as a lack of awareness and access to DTx programs in emerging markets, resistance from traditional healthcare providers, and uneven payment models, which are hindering its full potential.

Digital health also promises to revolutionise patient care, streamline operations, and enable unprecedented access to medical resources. Innovations including AI, and big data analytics are transforming the way healthcare providers diagnose, treat, and monitor patients. These technologies facilitate real-time data collection and analysis, personalised treatment plans, and improved patient engagement, and could lead to more efficient and effective healthcare delivery.

Changing the face of Parkinson's diagnosis with an AI-enabled IVD

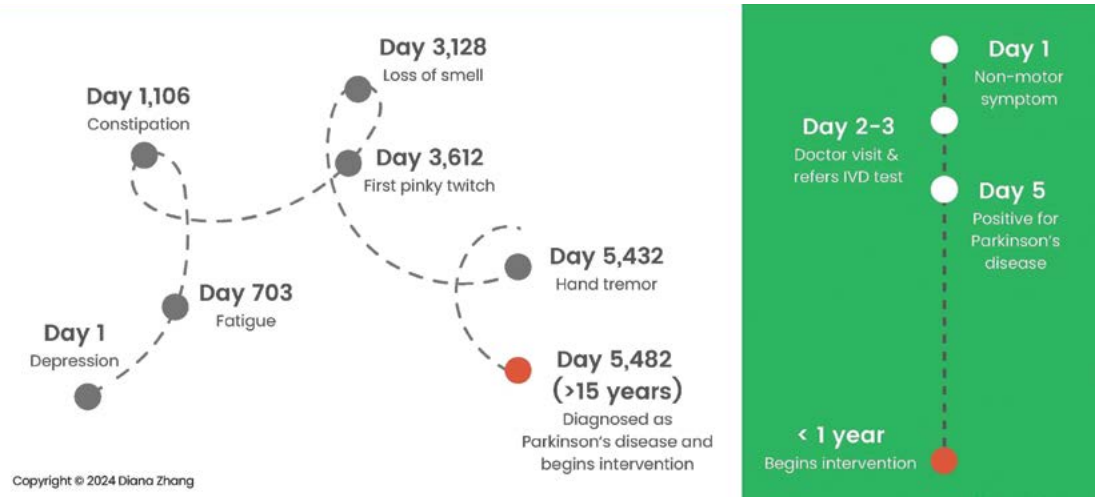
— Presenter: Dr Diana Zhang, Founder and CEO, Preview Health

AI holds transformative potential in medical technology, including in the diagnosis and treatment of Parkinson's disease. Currently, AI is employed to streamline labour-intensive tasks for doctors, but its true potential lies in achieving what was once considered impossible. A notable example is a woman who could detect Parkinson's disease through smell before clinical diagnosis. This inspired Dr Zhang's research that focused on using AI for early Parkinson's detection.

Parkinson's disease presents a significant challenge because by the time motor symptoms like tremors appear, up to 80% of normal brain function may already be lost. However, non-motor symptoms, such as anxiety and sleep disorders, can manifest decades earlier. Early intervention, including exercise, can help delay disease progression. Dr Zhang's research found that AI can analyse blood plasma metabolites and detect Parkinson's up to 15 years before clinical diagnosis with 96% accuracy. This innovation has sparked significant public interest.

The impact of early diagnosis on patients and their families is profound. An AI-enabled in vitro diagnostic (IVD) tool could reduce the suffering caused by late or incorrect diagnoses. For example, an Australian case reported that it took 16 years for her mother to be correctly diagnosed with Parkinson's. AI has the potential to revolutionise Parkinson's diagnosis, leading to timely interventions, reduced unnecessary testing, and lower healthcare costs. Additionally, early diagnosis could enhance drug development by allowing the enrolment of early-stage patients in clinical trials, potentially improving the efficacy of new treatments.

Figure 11. Changing the face of Parkinson's diagnosis with an AI-enabled IVD



Source: Published with permission from Dr Diana Zhang presentation; Horizon Scanning Forum 2024

Implications for the health system and patient access

The rate of digital health is escalating at a rapid rate. The digital health we have today will most likely be obsolete in 5 to 7 years. The issue we face is how we prepare to adopt this avalanche of innovation. Regulation, funding, workforce, training, patient acceptance, data interoperability, data access, storage and retrieval, privacy and security are all constraints that need to be addressed to allow fulsome use of the emerging technology.

Early detection and personalised care will benefit all stakeholders and can reduce health care costs. To better enable this, the health system needs to shift from an episodic and reactive model of 'sick care' to a more 'wellness' personalised healthcare journey, which is now possible with the emerging and disruptive digital health technologies.

> We need a shift in thinking from politicians to policy makers to taxpayers –to think of health as an investment, not an expense.
>
> – Olivia Nassaris, CEO Parkinson's Australia

HTA Review options: Digital health

Australia's healthcare system, known for its rigorous HTA processes, faces unique challenges and opportunities with the integration of digital health. The HTA framework ensures that only proven interventions are adopted. The rapid pace of digital innovation poses challenges for this system.

While the HTA Review Options Paper did not specifically focus on digital health, research papers developed for the HTA Review acknowledged these as emerging. The HTA Review Options Paper noted that the range of potential future technology types are too diverse to create further rigid pathways that delineate between different technology types and/or their intended outcome/s. It states the need for existing flexibility to be maintained to ensure that HTA can adapt to new health technology types that may be marketed in the future.

It must be acknowledged that the HTA review had several aims that are relevant to digital health:

1. Adopt a person-centred approach in HTA.
2. Progress the objectives of the new National Medicines Policy (NMP) (most notably, 'Equitable, timely, safe and affordable access to a high-quality and reliable supply of medicines and medicines-related services for all Australians'. The NMP also makes specific references to digital technologies).
3. Ensure HTA policy and methods are well adapted to and capable of assessing new technologies that are emerging or are expected to emerge in the coming years.

The traditional HTA process may struggle to keep up with the fast-evolving digital health landscape. A streamlined HTA process tailored for digital health innovations could expedite the adoption of beneficial technologies while maintaining rigorous standards.

Australia could benefit from the experience of other countries' HTA processes which have reimbursed digital health. For example, the UK's NICE initiated a new early value assessment approach to allow rapid assessment of digital health products, devices and diagnostics for clinical effectiveness and value for money. The stated goal of this process is so that patients in the UK can benefit from these promising technologies sooner.

Implications of an AI-enabled IVD on regulatory, reimbursement and health systems

— Presenter: Oona Reardon, Director, Pulse Economics Consulting

The application of AI-enabled IVDs is expected to expand to other neurological diseases, including Alzheimer's. However, challenges in regulatory approval and reimbursement are anticipated, suggesting a staged approach to implementation may be appropriate. AI enabled IVDs could initially replace positron emission tomography (PET) scans for diagnosing patients with motor symptoms. It could then be used prognostically for individuals with loss of smell or mild cognitive impairment, and eventually as a population screening tool.

The TGA may encounter uncertainties when evaluating AI software before granting regulatory approval. Addressing reimbursement challenges for AI-enabled IVD tools is crucial for their successful adoption and integration into healthcare systems. However, given the lack of disease-modifying therapies for conditions like Parkinson's disease (PD) and Alzheimer's, securing reimbursement for AI-enabled IVD tools as diagnostic devices presents additional hurdles. The MSAC's "Value of Knowing" criteria will be instrumental in justifying the psychological benefits of early diagnosis and the potential for enrolling early-stage patients in drug trials. The cost burden of Parkinson's disease is significant, with government expenditures of around $40,000 AUD per patient annually, including $11,000 AUD for hospital admissions related to medication adjustments.[41] Patients and caregivers also face substantial costs, mostly for informal home-based care.

An AI-enabled IVD tool could facilitate earlier and more accurate diagnoses, reducing unnecessary tests and inappropriate treatments. An Australian study found that approximately half of patients receiving anti-Parkinson medication do not have the disease,[42] indicating potential savings for the healthcare system. As disease-modifying therapies become available, a reduction in hospitalisations and medical services is expected. Promising results have been observed in drugs like exenatide, currently in phase three trials for Parkinson's disease. The integration of AI technology is poised to significantly transform neurodegenerative care, making advanced diagnostics and treatments more accessible and effective.

> "We need to move towards a more predictive, preventative and personalised healthcare system, and we already have a lot of what we need to start this journey."
>
> – Dean Whiting, CEO PTA

Theme 2. A co-designed horizon scanning process would help to identify unmet needs and enable system readiness to support timely access to new therapies

Gearing up for change – reforming the system and the role of horizon scanning
Dr Anna Lavelle AM, Medicines Australia Chair
Urs Voegeli, Managing Director J&J
Dr Paul Fennessey, Horizon scanning expert with state health system experience

Facilitator: Liz de Somer, CEO Medicines Australia

Wrap up and closing remarks
DoHAC and Medicines Australia

2.1 Future of horizon scanning in Australia

Horizon scanning is critically important to help operational, capability and capacity planning for HTA and health systems. Horizon scanning may also identify potential legislative changes as well as resources, systems and process changes needed in preparation for the introduction of therapeutic advances and other disruptive technologies.

> Horizon scanning needs to focus on future problems as well, not just future solutions.
>
> – Prof Paul Kelly, Chief Medical Officer

The establishment of Medicines Australia's annual Horizon Scanning Forum marks a step forward. However, for horizon scanning to be truly transformative and set Australia up for the future, a comprehensive commitment and allocation of resources from all levels of government is essential. Further, co-designing with key stakeholders will be needed for a robust horizon scanning framework in Australia. While Australia does not currently have a nationally coordinated horizon scanning system, the annual Horizon Scanning Forum has highlighted the value of horizon scanning for system awareness and preparedness.

Existing models

To develop and implement a more robust and inclusive horizon scanning system Australia can look to other countries where horizon scanning is well established, and adapt an Australian-specific horizon scanning system from learnings in those countries.

Canada and the UK have both invested significantly in horizon scanning over the decades, leading to robust systems. In Canada, horizon scanning has historically been a key function, but recent shifts towards establishing a national drug formulary have redirected focus away from horizon scanning. This shift may have led to a reduced emphasis on horizon scanning at the national level, although some provinces have maintained or increased their horizon scanning efforts to fill this gap.

In the UK, the NICE initially focused its horizon scanning efforts on pharmaceuticals, with notable success. The University of Birmingham played a significant role by establishing a strong relationship with industry, including non-disclosure agreements to gain early access to information. This approach enabled the development of detailed horizon scanning documents that informed NICE's decision-making. However, since then, the horizon scanning function has moved to Newcastle, broadening its scope to include a wider range of healthcare innovations and unmet needs, such as addressing the needs of an ageing population.

Post the COVID-19 pandemic, there has been a noticeable shift in how horizon scanning is approached globally. With fewer resources and increased demands on agencies, there is a push to reinvent methodologies to be more efficient and focused. The challenge is to provide valuable insights to decision-makers and healthcare providers without overwhelming them with excessive information.

The question arises whether horizon scanning should be tailored to national priorities and unique challenges, or if challenges are universally similar. While evidence used in horizon scanning may be similar across different regions, the application and interpretation of this evidence are context specific. Thus, while global trends and practices provide a useful framework, tailoring horizon scanning to address local priorities and avoid duplication is essential.

The experiences of Canada and the UK illustrate the evolution and adaptation of horizon scanning systems. While these systems have faced shifts and challenges, learning from their methods—such as establishing strong industry relationships and focusing on both broad and specific healthcare needs—can guide the development of effective horizon scanning processes.

Alternatively, Australia could learn from its own National Health Genomics Policy (NHGP) Framework as a template for implementing a robust horizon scanning process. The NHGP provides direction for governments in Australia to integrate genomics into our health system. It uses an agreed high-level national approach to policy, regulatory and investment decision-making for genomics.[43]

Patient voice

The contribution of consumers and patients in the horizon scanning process is significant and beneficial. This includes early involvement of consumers/ patients to allow for better shared understanding and knowledge of what the medical intervention can provide for them. Patient advocacy organisations are already doing a lot of work in horizon scanning. Consolidating, co-ordinating and harmonising these efforts will enhance their impact. This could be achieved if the patient voice is included in a co-designed horizon scanning process for Australia.

Establishing a national horizon scanning mechanism would undoubtedly improve communication and preparedness across different sectors and jurisdictions. This will require cooperation between governments, industry, and other stakeholders.

> Relevance is the key value in allowing consumer/ patient involvement. Trying to develop a health system without a consumer, is like building a house without talking to the owner.
>
> – Ann Single, Patient Advocate

Theme 3. The HTA Review has provided some good options to take horizon scanning forward in partnership.

The value of horizon scanning has been well acknowledged in the HTA Review Options Paper. It includes proposals for the "establishment of horizon scanning programs to address specific informational needs within HTA and the health system". Specific options proposed in the paper included horizon scanning:

- For advanced therapies (including high cost, Highly Specialised Therapies funded through the NHRA) and other potentially disruptive technologies.
- To meet priority areas (including addressing equity and high unmet clinical need).
- To help operational and capacity planning for HTA and health systems.

Medicines Australia supports all three options for horizon scanning and believes they should be, and can be, implemented as they are complementary. These adoptions could have implications for the Commonwealth when considering the introduction of therapeutic advances. Thus, it will also be necessary to consider potential legislative, resource, systems and process changes.

Conclusion

The growing demand on the healthcare system from an ageing population with increasingly complex health conditions, necessitates urgent reforms to the funding of medicines, vaccines, biotherapeutics and digital health. The HTA Review and the Horizon Scanning Forum engaged a broad range of key stakeholders, including patients, health care providers, researchers, policy makers and industry, who together have the common goal of ensuring a sustainable and effective healthcare system, for current and future generations of Australians.

Discussion across each of the four therapeutic areas highlighted the need and potential benefit of a nationally coordinated horizon scanning system and process, and the urgent need for broader HTA reforms, so Australia can capitalise on the full potential of accelerating innovations in medicines, vaccines and biopharmaceuticals.

Medicines Australia supports the coordinated implementation of all three horizon scanning priorities proposed in HTA Review Options Paper. Medicines Australia will continue to work in partnership with the Government to progress horizon scanning, and keep stakeholders informed of major therapeutic advances as we move through this remarkable new era of medical research and therapy development.

Chris Bond shared his experience of AMR with the audience

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